RESTRICTION REQUIREMENT

Applicants thank the Examiner for the courtesy of an interview on March 4, 2003, and gratefully acknowledge the Examiner's efforts to promote the prosecution of the present application. The possible reformatting of the restriction requirement was discussed during the interview and alternative restriction requirements were considered by both the Examiner and Applicants' representative.

One alternative restriction discussed during the March 4, 2003 interview is as follows: group 1 -- comprising claims 1-19, 26-47, comprising diarylsulfide compounds of formula (I) and (III), and compositions comprising the same, which may optionally be subdivided at the Examiner's discretion into two groups according to presence or absence of a heterocyclic moiety anywhere on the compound; group 2 -- comprising claim 24, comprising diarylsulfide compounds of formula (II); group 3 -- comprising claims 52-60, comprising diarylsulfide compounds which bind to the interaction domain of LFA-1; group 4 -- comprising claim 25, comprising a method of preparing a compound of formula (II); group 5 -- comprising claims 20-21 and 48, comprising a method of inhibiting inflammation; group 6 -- comprising claims 22-23, comprising a method of suppressing immune response; group 7 -- comprising claims 49-51, comprising a method of treating an inflammatory condition.

If the Office decides to continue examination of the application using this alternative restriction, Applicants elect the alternate group 1 and elect the species [3-(3-carboxypiperidin-1-yl)phenyl] [2,3-dichloro-4-(E-((4-morpholino)carbonyl) ethenyl)phenyl]sulfide. The specification discloses the elected species in Example 399,

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page 349, line 13, to page 350, line 7, and in claim 12, page 461, lines 1-2. At least claims 1, 3-4, 6, 8, 10-12, 16, 18-23, and 26-60 read on the elected species.

Applicants respectfully submit that the alternative restriction requirement is a manageable and meaningful way to divide the claimed subject matter. Further, the alternative restriction groups suggested above do not pose a serious burden on the Office. Accordingly, Applicants respectfully request that the Office consider reformatting the current restriction groups as was discussed in our interview of March 4, 2003.

If, however, the Office does not reformat the pending restriction groups, then Applicants maintain their traversal of the pending restriction requirement for reasons of record, and on the ground that there has been no showing that either of the two necessary criteria for a restriction requirement, i.e., (1) that the groups restricted are patentably distinct, and (2) that there would be a serious burden to examine the claims of Groups I-VII together. M.P.E.P. § 803.

The groups are not patentably distinct because the groups as set forth contain certain overlaps. See, for example, the Office's exemplary species of Group I, 386, 401, and 410, are also stated to fall within Groups II (410) or III (386 and 401.) (Office Action, pages 2-3.) Therefore, Applicants respectfully submit that the search for each of these groups would be co-extensive and there would be no serious burden in examining the restricted groups together.

The Office indicated that the previous elected species falls within original Group II. (Office Action, page 4.) It is Applicants' understanding that Group II encompasses the subject matter, comprising claims 1, 3-23, 26-60 (in part), drawn to a compounds, compositions and a method of use, wherein R3 comprises a cinnamide and wherein

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one of the R3-cinnamide and Ar groups comprises a 6-membered heterocycle containing nitrogen and additionaly 1-3 heteroatoms.

Upon allowance of a generic claim, Applicants note that rejoinder of process claims that depend from or otherwise include all the limitations of the allowed claim should be entered as a matter of right. M.P.E.P. § 821.04.

DOUBLE PATENTING

Claims 1, 3-23, and 26-60 were rejected for double patenting as unpatentable over U.S. Patent No. 6,110,922 and co-pending Application No. 09/695,040. (Office Action, page 5.) Regarding the rejection over U.S. Patent No. 6,110,922, it is Applicants' understanding that the Examiner has modifed the statutory double patenting rejection and made it a non-statutory obviousness-type double patenting rejection that is curable by filing a terminal disclaimer. If the Examiner has not withdrawn the statutory §101 double patenting rejection then Applicants reaffirm their traversal that the claims are not of identical scope. Although Applicants disagree with the rejections for reasons of record, they request that the rejections be held in abeyance until allowable subject matter is indicated.

ENABLEMENT REJECTIONS

The Examiner indicated during the interview of March 4, 2003, and as stated in the interview summary, that the enablement rejection under 35 U.S.C. § 112, first paragraph, is applied only against the methods of use claims. Accordingly, the Office is asserting the enablement rejection only against claims 20-23 and 48-51.

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Claims 20-23 and 48-51 remain rejected under 35 U.S.C. § 112, first paragraph, for non-enablement for reasons of record. (Office Action, page 6.) Applicants traverse this rejection for reasons of record, and as supplemented herein.

All patent applications are presumptively adequate, *In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971), and the Office must accept as true Applicants' statements set forth in the specification, "unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." M.P.E.P § 2164.04.

As a basis for the rejection, the Office alleges that the that "[t]he specification does not give any guidance as to the method for suppressing immune response by way of inhibitory activity in an ICAM/LFA-1 biochemical interaction or ICAM-3/JY-8 cell adhesion [assay] for treating a mammal suffering from a generic inflammation disorder ...[by] administering a composition...from claim 19 or 47." (Office Action dated February 27, 2002, page 14.) First, Applicants point out that specific working examples need not be disclosed to provide an enabling disclosure (M.P.E.P § 2164.02). The instant specification does, in fact, disclose examples for using the claimed compounds for inhibiting an ICAM-1/LFA-1 biochemical interaction, for inhibiting ICAM-1/JY-8 cell adhesion, and for inhibiting ICAM-3/JY-8 cell adhesion. See page 404, line 1, to page 411, line 21. Also, one of skill in the art reading the specification, for example, pages 412-415, would know that the specification provides sufficient guidance to use the claimed compounds and compositions for treating a specific disorders or diseases. Furthermore, given the skill in the art of small molecule pharmaceuticals at the time of

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filing, the skilled artisan would know that the claimed methods would not require undue experimentation to use the small molecules for uses known in the art.

Second, the Federal Circuit has held that data from an *in vitro* model or an animal model can support claims directed to therapeutic methods if the art is such that a particular model is recognized as correlating with a particular condition. In re Brana, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). If this correlation exists, then an *in vitro* model or an animal model example in the specification constitutes a working example of the claimed method. M.P.E.P. § 2164.02. Furthermore, a rigorous correlation need not be shown -- a reasonable correlation suffices. Fujikawa v. Wattanasin, 39 U.S.P.Q.2d 1895, 1990 (Fed. Cir. 1996), citing Nelson v. Bowler, 206 U.S.P.Q. 881 (C.C.P.A. 1980). See also, Cross v. Iizuka, 224 U.S.P.Q. 739, 747 (Fed. Cir. 1985) (holding that a rigorous correlation is not necessary where the disclosure of pharmaceutical activity is reasonable based upon the probative evidence). Applicants point out that the specification discloses that the compounds were tested in vitro and that they have biological activity (page 406, lines 1-2, page 407, lines 13-14, and page 409, lines 6-7.) The specification also discloses numerous methods for using the inventive compounds for treating specific disorders and diseases (page 412-416) Moreover, Applicants submit that one of skill in the art reading the specification would know that the biological activity of the claimed compounds reasonably correlates with the disclosed methods of use. Therefore, Applicants submit that the disclosure enables the methods of using the claimed compounds and compositions.

In addition, the Office has provided five (5) additional references regarding the state of the art: (1) Zhou et al. (PubMed Abstr.:11776041) uses SOD injection for

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treating polyarthritis; (2) Pillinger et al. (PubMed Abstr.: 9826736) studies different modes of action for structures different from the claimed compounds; (3) Emond et al. (PubMed Abstr.: 11881994) investigates diphenyl sulfides as serotonin transporter ligands; (4) Fujita et al. (PubMed Abstr.: 11408364) selectively inhibiits CYP2A6 by 4,4'pyridyl disulfide; and (5) Kelly et al. (PubMed Abstr.: 10553036) allegedly antagonizes LFA-1 adhesion with low m.w. molecules other than diphenyl sulfide derivatives. (Office Action, pages 6-8.) The references do not disclose the claimed compounds or compositions. Nor does the Office indicate how these references support its allegation that the claimed methods would require undue experimentation in view of the Applicants' disclosure and the skill in the art at the time of filing. Applicants submit that the claims are enabled by the specification, and that these additional references do not support the Office's allegation that the skilled artisan would require undue experimentation to enable the claimed methods.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the enablement rejections.

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